ITPR1 gene

inositol 1,4,5-trisphosphate receptor type 1

Normal Function

The *ITPR1* gene provides instructions for making a protein that is part of a channel that controls the flow of positively charged calcium atoms (calcium ions) within cells. Four ITPR1 protein molecules join together in a complex (a homotetramer) to form the channel. In response to certain signals, the ITPR1 channel releases calcium ions from storage in a cell structure called the endoplasmic reticulum into the surrounding cell fluid (the cytoplasm). Proper regulation of calcium ion concentration inside cells is important for the development and function of various tissues and organs.

Health Conditions Related to Genetic Changes

Gillespie syndrome

At least 13 *ITPR1* gene mutations have been identified in people with Gillespie syndrome, a disorder that involves eye abnormalities, weak muscle tone from birth (congenital hypotonia), problems with balance and coordinating movements (ataxia), and mild to moderate intellectual disability. The *ITPR1* gene mutations that cause Gillespie syndrome likely result in a protein with an altered structure. It is thought that calcium channel homotetramers made with the altered proteins are unstable. A shortage of normal ITPR1 channels impairs the cell's ability to regulate the concentration of calcium ions. However, the specific connection between these changes and the signs and symptoms of Gillespie syndrome is unclear.

Other disorders

Mutations in the *ITPR1* gene have been identified in people with spinocerebellar ataxia type 15 (SCA15), spinocerebellar ataxia type 29 (SCA29), and less commonly, in other forms of spinocerebellar ataxia. These conditions lead to movement problems that worsen over time. The mutations associated with these disorders likely impair regulation of calcium levels in cells, leading to the signs and symptoms of spinocerebellar ataxia.

Researchers are working to understand why some people with *ITPR1* gene mutations have only movement problems while others also have the eye problems and intellectual disability characteristic of Gillespie syndrome (described above). Studies indicate that *ITPR1* gene mutations that cause the spinocerebellar ataxias affect different regions of

the protein than do the mutations that cause Gillespie syndrome. The mutations may also differ in the degree to which they destabilize the homotetramer structure of the calcium channel. These factors could account for the different patterns of signs and symptoms among Gillespie syndrome and the various spinocerebellar ataxias.

Other Names for This Gene

- IP3R
- IP3R1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ITPR1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3708[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ITPR1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SPINOCEREBELLAR ATAXIA 29; SCA29 (https://omim.org/entry/117360)
- INOSITOL 1,4,5-TRIPHOSPHATE RECEPTOR, TYPE 1; ITPR1 (https://omim.org/entry/147265)
- SPINOCEREBELLAR ATAXIA 15; SCA15 (https://omim.org/entry/606658)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3708)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ITPR1[gene])

References

- Dentici ML, Barresi S, Nardella M, Bellacchio E, Alfieri P, Bruselles A,Pantaleoni F, Danieli A, Iarossi G, Cappa M, Bertini E, Tartaglia M, Zanni G.Identification of novel and hotspot mutations in the channel domain of ITPR1 intwo patients with Gillespie syndrome. Gene. 2017 Sep 10;628:141-145. doi:10.1016/j.gene.2017.07.017. Epub 2017 Jul 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/28698159) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5607352/)

- Gerber S, Alzayady KJ, Burglen L, Bremond-Gignac D, Marchesin V, Roche O, RioM, Funalot B, Calmon R, Durr A, Gil-da-Silva-Lopes VL, Ribeiro Bittar MF, OrssaudC, Heron B, Ayoub E, Berquin P, Bahi-Buisson N, Bole C, Masson C, Munnich A,Simons M, Delous M, Dollfus H, Boddaert N, Lyonnet S, Kaplan J, Calvas P, YuleDI, Rozet JM, Fares Taie L. Recessive and Dominant De Novo ITPR1 Mutations CauseGillespie Syndrome. Am J Hum Genet. 2016 May 5;98(5):971-980. doi:10.1016/j.ajhg.2016.03.004. Epub 2016 Apr 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27108797) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4863566/)
- Hall HN, Williamson KA, FitzPatrick DR. The genetic architecture of aniridiaand Gillespie syndrome. Hum Genet. 2019 Sep;138(8-9):881-898. doi:10.1007/s00439-018-1934-8. Epub 2018 Sep 22. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/30242502)
- McEntagart M, Williamson KA, Rainger JK, Wheeler A, Seawright A, De Baere E, Verdin H, Bergendahl LT, Quigley A, Rainger J, Dixit A, Sarkar A, Lopez Laso E, Sanchez-Carpintero R, Barrio J, Bitoun P, Prescott T, Riise R, McKee S, Cook J, McKie L, Ceulemans B, Meire F, Temple IK, Prieur F, Williams J, Clouston P, Nemeth AH, Banka S, Bengani H, Handley M, Freyer E, Ross A; DDD Study; vanHeyningen V, Marsh JA, Elmslie F, FitzPatrick DR. A Restricted Repertoire of DeNovo Mutations in ITPR1 Cause Gillespie Syndrome with Evidence forDominant-Negative Effect. Am J Hum Genet. 2016 May 5;98(5):981-992. doi:10.1016/j.ajhg.2016.03.018. Epub 2016 Apr 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27108798) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4863663/)

Genomic Location

The *ITPR1* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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